

REMARKS

The Applicants wish to sincerely thank the Examiner for granting a telephone interview on June 1, 2005.

Amendments to the Specification

Twelve paragraphs of the specification were amended for correction of typographical errors, grammatical reasons or clarity. The Applicants hereby state that all amendments do not add new subject matter to the specification. Specifically, the specification was amended as follows:

1. The amendment of paragraph page 1, lines 22-25 through page 2, lines 1-9 replaces a less than sign with a greater than sign on page 2, line 3. This was a typographical error.
2. The amendments of paragraph page 3, lines 1-21 replaces "unregulated" with "upregulated" in line 7 and adds "current" to line 17. These were typographical errors.
3. The amendments of paragraph page 4, lines 6-16 deletes "blocker" at both locations in line 8, replaces "florescent" with "fluorescent" in both locations in line 10, replaces "K" with "K⁺" in line 9 and replaces "AtPase" with "ATPase" in line 9. These were typographical errors. In addition, the amended paragraph deletes "a" in both locations in line 8, replaces "demonstrate" with "demonstrates" in line 8, replaces "current" with "currents" in line 8 and adds "also" in line 9 for grammatical reasons.
4. The amendment of paragraph page 5, lines 10-13 deletes "showing a combination of inactivating Na⁺ channels." in line 11 for grammatical reasons.
5. The amendments of paragraph 6, lines 3-12 replaces "depolarization" with "hyperpolarization" in line 4, replaces "K" with "K⁺" in line 8 and line 9 and replaces "E_{Na}" with "E_{Na}". These were typographical errors. In addition, "between" was added in line 8 for grammatical reasons.
6. The amendments of paragraph 6, lines 13-23 replaces "K" with "K⁺" in line 15 and line 21 and "K" with "K⁺," in line 21. These were typographical errors.
7. The amendments of paragraph on page 8, lines 17-23 through page 9, lines 1-3 subscripts the "2" in CaCl₂ and MgCl₂ on page 8, line 20, replaces "K" with "K⁺" on page 8, line 21 and replaces "K" with "K⁺" on page 9, line 1. These were typographical errors. In addition, the amended paragraph replaces "contains" with "contain" on page 8, line 19 for grammatical reasons.
8. The amendments of paragraph on page 9, lines 19-23 through page 10, lines 1-12 replaces "K" with "K⁺" on page 9, line 22, on page 9, line 23, on page 10, line 3, on page 10, line 5 and on page 10, line 7. These were typographical errors. In addition the sentence "Under these conditions blocking noninactivating Na⁺ channels (these remain open) will hyperpolarize the membrane towards the equilibrium potential for K.", beginning on page 10, line 3 was rewritten "Under these conditions noninactivating Na⁺ channels remain open and depolarize the cell membrane. Thus, blocking the

noninactivating Na⁺ channels will hyperpolarize the membrane towards the equilibrium potential for K⁺." for clarity.

9. The amendments of paragraph on page 10, lines 13-17 replaces "K" with "K⁺" in line 14 and deletes "the" in line 16. These were typographical errors. In addition, the amended paragraph replaces "the final" with "a" in line 13 for clarity.
10. The amendments of paragraph on page 10, lines 18-23 through page 11, lines 1-7 replaces "K" with "K⁺" on page 10, line 21, twice on page 11, line 3 and on page 11, line 5 and replaces "Cl" with "Cl⁻" on page 11, line 1. These were typographical errors.
11. The amendments of paragraph on page 11, lines 14-22 through page 12, lines 1-2 adds a period to the sentence ending on page 11, line 4 for grammatical reasons.
12. The amendments of the Abstract on page 19, lines 3-11 deletes "blocker" in line 4, replaces "K" with "K⁺" in line 5, replaces "AtPase" with "ATPase" in line 5, and replaces "florescent" with "fluorescent" in line 5 and line 6. These were typographical errors.

Amendments to the Claims

The Applicants respectfully ask the Examiner to replace all prior versions and listings of claims in the instant application with the listing of claims currently provided. Claims 1-10 were canceled and Claims 11-46 are new.

1. Support for the method embraced by Claims 11 and 25 and the claims depending from these two independent claims can be found on page 4, lines 6-22; page 5, lines 14-22 through page 6, lines 1-2; page 7, lines 4-23; page 8, lines 17-23 through page 9, lines 1-18; Abstract and FIG. 2.

Specifically, support for the method components of step (a) of Claims 1 and 25 are as follows:

- a. "a Na⁺-free physiological buffer" can be found, *e.g.*, on page 5, line 21 and on page 8, lines 18-20.
- b. "a voltage-sensitive fluorescence dye" can be found, *e.g.*, on page 4, lines 21-22; and page 7, lines 16-20; and page 19, lines 5-6.
- c. "a cell having a K⁺ channel, a transient Na⁺ channel and a persistent Na⁺ channel" can be found, *e.g.*, on page 4, line 18-21; page 7, lines 4-14; and page 8, lines 8-16.
- d. "a potential Na⁺ channel blocker" can be found, *e.g.*, on page 4, lines 12-15; and page 9, lines 12-18.

Support for the method steps (b-i) of Claims 1 and Claim 25 are as follows:

- a. step (b): "depolarizing membrane of the cell in the test sample 1" can be found, *e.g.*, on page 5, line 22; and page 8, lines 20-23 through page 9, lines 1-3.
- b. step (c): "generating a current through the persistent Na⁺ channel by adding Na⁺ to test sample 1 at least 10 msec after step (b)" can be found, *e.g.*, on page 6, lines 1-2; and page 9, lines 4-11.

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- c. step (d): "detecting fluorescence emitted by the voltage-sensitive dye in test sample 1" can be found, *e.g.*, on page 4, lines 9-16; page 7, lines 14-20; and page 19, lines 6-7.
- d. steps (e-i): support for a parallel assay using a control sample can be found, *e.g.*, on page 6, lines 1-2; page 9, lines 4-11.

Support for the method steps (j-q) of Claim 1 can be found, *e.g.*, on page 9, lines 12-18; and page 11, lines 8-22 through page 12, lines 1-8.

Support for Claim 25 and screening for a persistent Na⁺ blocker can be found, *e.g.*, on page 9, lines 12-13.

- 2. Support for the method embraced by Claims 36 and 41 and the claims depending from these two independent claims can be found, *e.g.*, on page 6, lines 3-12; page 9, lines 19-23 through page 10, lines 1-12; Abstract and FIG. 3.

Specifically, support for the method components of step (a) of Claims 36 and 41 are as follows:

- a. "a physiological buffer" can be found, *e.g.*, on page 6, lines 9-11.
- b. "a voltage-sensitive fluorescence dye" can be found, *e.g.*, on page 4, lines 21-22; page 7, lines 16-20; and page 19, lines 5-6.
- c. "a cell having a K⁺ channel and a persistent Na⁺ channel wherein a resting membrane potential of the cell is approximately halfway between an equilibrium potential of Na⁺ and an equilibrium potential of K⁺" can be found, *e.g.*, on page 6, lines 7-9; page 9, lines 20-23 through page 10, lines 1-5; and FIG. 3.

Support for the method steps (b-e) of Claim 36 and Claim 41 are as follows:

- a. steps (b and d): "detecting fluorescence emitted by the voltage-sensitive dye in test sample 1" can be found, *e.g.*, page 4, lines 9-16; and page 7, lines 14-20.
- b. step (c): "adding a potential Na⁺ channel blocker to test sample 1" can be found, *e.g.*, on page 4, lines 12-15; page 6, lines 11-12; and page 10, lines 10-12.
- c. steps (e): "determining a relative emitted fluorescence 1 by comparing the emitted fluorescence from step (b) with the emitted fluorescence from step (d)" can be found, *e.g.*, on page 10, lines 5-12; and page 19, lines 6-7.

Support for the method steps (f-m) of Claim 36 can be found, *e.g.*, on page 9, lines 12-18; and page 11, lines 8-22 through page 12, lines 1-8.

Support for Claim 41 and screening for a persistent Na⁺ blocker can be found, *e.g.*, on page 9, lines 12-13.

- 3. Support for the method embraced by Claims 43 and 45 and the claims depending from these two independent claims can be found, *e.g.*, on page 6, lines 13-23; page 10, lines 13-23 through page 11, lines 1-7 Abstract and FIG. 4.

Specifically, support for the method components of step (a) of Claims 43 and 45 are as follows:

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- a. "a Cl⁻-free physiological buffer" can be found, *e.g.*, on page 6, line 19-21; and page 11, lines 1-3.
- b. "a voltage-sensitive fluorescence dye" can be found, *e.g.*, on page 7, lines 16-20; and page 19, lines 5-6.
- c. "a cell having a K⁺ channel and a persistent Na⁺ channel wherein a K⁺ conductance of the K⁺ channel is at least 50-fold higher than a Na⁺ conductance from the persistent Na⁺ channel" can be found, *e.g.*, on page 6, lines 14-17; and page 10, lines 14-17.
- d. "a potential Na⁺ channel blocker" can be found, *e.g.*, on page 4, lines 12-15; on page 6, lines 22-23; and page 11, lines 6-7.

Support for the method steps (b-g) of Claim 43 and Claim 45 are as follows:

- a. step (b): "depolarizing membrane of the cell in the test sample 1" can be found, *e.g.*, on page 6, lines 13-14; page 6, lines 17-22; and page 10, lines 18-22 .
- b. step (c) "detecting fluorescence emitted by the voltage-sensitive dye in test sample 1" can be found, *e.g.*, on page 4, lines 9-16; page 7, lines 14-20; and page 19, lines 6-7.
- c. steps (d-g): support for a parallel assay using a control sample can be found, *e.g.*, on page 6, lines 17-23; page 10, lines 22-23 through page 11, lines 1-7.

Support for method steps (h-o) of Claim 43 can be found, *e.g.*, on page 9, lines 12-18; and page 11, lines 8-22 through page 12, lines 1-8.

Support for Claim 45 and screening for a persistent Na⁺ blocker can be found, *e.g.*, on page 9, lines 12-13.

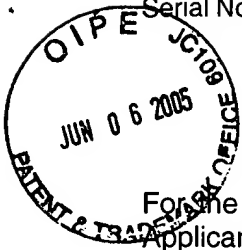
Rejection Pursuant to 35 U.S.C. §112, ¶2 Indefiniteness

The Examiner has rejected Claims 6-10 as allegedly lacking definiteness under 35 U.S.C. §112, ¶2. The Applicants respectfully submit that cancellation of Claims 6-10 renders the indefiniteness rejections directed towards these claims as immaterial, and thus are not addressed in the Applicant's Reply.

Rejection Pursuant to 35 U.S.C. §102(e) Anticipation

The Examiner has rejected Claims 6, 9 and 10 as allegedly anticipated under 35 U.S.C. §102(b) by U.S. Patent 6,686,193, Michael P. Maher and Jesus E. Gonzalez, High Throughput Method and System for Screening Candidate Compounds for Activity Against Target Ion Channels (Feb. 3, 2004). The Applicants respectfully submit that cancellation of Claims 6-10 renders the indefiniteness rejections directed towards these claims as immaterial, and thus are not addressed in the Applicant's Reply.

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CONCLUSION

For the above reasons the claims are now thought to be in condition for allowance, and the Applicants respectfully urge the Examiner to issue a Notice to that effect. Please use Deposit Account 01-0885 for the payment of the extension fees or any other fees due in connection with the current response.

Respectfully submitted,

A handwritten signature in dark ink, appearing to read "Dean G. Stathakis", followed by a long horizontal flourish.

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